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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/349,194	07/07/1999	KENNETH F. BUECHLER	244/121	6285

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	22

DATE MAILED: 09/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/349,194	BUECHLER ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-96,102-106 and 114-142* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-96,102-106 and 114-142* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response, filed 5/17/02 in Paper No. 21 are acknowledged and has been entered. Claims 87, 88, 90, 93, 96, 105, 116-119, 121-124, 126-129, and 131-133 have been amended. Currently, claims 85-96, 102-106, and 114-142 are pending and are under examination.

Rejection Withdrawn

2. In light of Applicant's amendment, the rejection of claims 124-125 and 141 under 35 U.S.C. 102(b) as being anticipated by Bodor et al. (Clinical Chemistry, 1992), is hereby, withdrawn.

3. In light of Applicant's amendment, the rejection of claims 126-128 under 35 U.S.C. 103(a) as being unpatentable over Bodor et al. (Clinical Chemistry, 1992), is hereby, withdrawn.

4. In light of Applicant's amendment, the rejection of claims 129-133 and 142 under 35 U.S.C. 103(a) as being unpatentable over Katus et al. in view of Bodor et al. (Clinical Chemistry, 1992), is hereby, withdrawn.

5. In light of Applicant's submission of a Terminal Disclaimer, the rejection of claims 85-96, 102-106, and 114-142 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-5, 8, 10-12, 14-18 of U.S. Patent No. 5,795,725, is hereby, withdrawn.

6. In light of Applicant's amendment and arguments, the rejection of claims 85-96, 102-106, and 114-142 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 85-96, 102-106, and 114-142 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for an assay for determining free and complexed cardiac specific isoforms of troponin (cTn) using a cocktail of antibodies, each having specific binding for free cTnI, binary complex of cTn, and ternary complex of cTn, does not reasonably provide enablement for an assay for determining free and complexed cTn using an antibody, i.e. single antibody, having specific binding for each and all of free cTnI, binary complex of cTn, and ternary complex of cTn. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the

invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for determining the presence or amount of all free and complexed isoforms of cTn using a cocktail of antibodies having specific binding for each and all of free, binary complex, and ternary complex isoforms of cTn.

The state of the prior art- the prior art of record fails to disclose a method for determining the presence or amount of all free, binary and ternary complexed isoforms of cTn using an antibody having specific binding for each and all of the free, binary, and ternary complexed isoforms of cTn.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the presence or amount of all of the free, binary and ternary complexed isoforms of cTn in a sample can be determined using an antibody wherein the antibody has specific binding for each and all of the free, binary, and ternary complexed isoforms of cTn.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed method to determine the presence or amount of all of the free, binary and ternary complexed isoforms of cTn in a sample using a cocktail of antibodies that have been generated to specifically bind one of the free, binary, and ternary complexed isoforms of cTn. However, the specification fails to provide any

guidance to enable the claimed method to make and use an antibody that specifically binds all of the free, binary and ternary complexed isoforms of cTn in a sample to determine the total concentration of a cTn isoform.

The presence or absence of working examples- working examples are provided in the specification that show that all of free and complexed isoforms of cTn can be determined in a sample using a cocktail of antibodies that specifically bind each of the free, binary, and ternary complexed isoforms of cTn. There are no working examples that show analogous results using an antibody, which is encompassed by the broad scope of the instant claims.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a method that is capable of determining the presence or amount of all free, binary, and ternary complexed isoforms of cTn. As recited, the instant method is capable of determining the presence or amount of all of free, binary, and ternary complexed isoforms of cTn using a single antibody that has specific binding for each of the free, binary, and ternary complexed isoforms of cTn.

In this case, the specification at pages 6-7 describes antibodies for use in the claimed method that are monoclonal, polyclonal, fragment thereof, and recombinant . These antibodies are characterized as being "sensitive" or "insensitive", the sensitive antibodies tend to bind and exhibit preferential detection of a single form of troponin and

the insensitive antibodies tend to bind and exhibit detection of more than one form of troponin. In pages 13-14, the specification shows that an insensitive antibody is utilized to bind to the free and complexed forms of troponin; that is, insensitive with respect to the oxidized, reduced, and complexed forms of troponin. Alternatively, more than one sensitive antibody would be necessary to measure both the free and complexed forms of troponin. At pages 21-22, the specification shows how to generate and select antibodies that are sensitive or insensitive to the binding of free troponin I or T, troponin I or T in binary complexes, and troponin I or T in ternary I/T/C complexes; this is accomplished by purification of free troponin I or T, binary troponin I/T, T/C, and I/C complexes and ternary I/T/C complexes, respectively, then injection into mice or rabbits to generate monoclonal or polyclonal antibodies. The antibodies are then screened for affinity and specificity with the purified free troponin, binary complexes of troponin, and ternary complexes of troponin.

While the specification at pages 29-31 exemplifies using selected antibodies, i.e. a cocktail of antibodies, that bind each of free cTn, binary complexed cTn, and ternary complexed cTn, in the claimed method of determining the amount of free, binary complexed, and ternary complexed cTn, the specification does not show any working examples of the claimed method using an antibody that has specific binding for all of the free cTn, binary complexed cTn, and ternary complexed cTn. The fact that insensitive antibodies that bind more than one form of cTn has been characterized, is not sufficient to enable the breadth of the claimed method to use a single insensitive antibody in an assay to determine the presence or amount of all of free cTn, binary complexed cTn,

and ternary complexed cTn. The specification does not establish a direct correlation between using a cocktail of insensitive and/or sensitive antibodies and a single "insensitive" antibody, which would lead the skilled artisan to say that the claimed method works for a single insensitive antibody to enable the breadth of the claimed method. The specification does not provide any teaching that suggests that an antibody generated against purified free cTn, an antibody generated against purified binary complexed cTn, or an antibody generated against purified ternary complexed cTn, can be characterized to bind a conserved epitope for each and all of said free cTn, binary complexed cTn, and ternary complexed cTn in a sample. Further, the working examples at Example 15 and Example 16, also utilize a cocktail of antibodies to determine the presence or amount of all of free cTn, binary complexed cTn, and ternary complexed cTn in a sample. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification. Thus, the claimed method is only enabled for use with a cocktail of antibodies having binding specificity for each of free cTn, binary complexed cTn, and ternary complexed cTn.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed method using a single antibody, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method would work using a single

insensitive antibody; 3) there is no proper guidance that shows that a single insensitive antibody has been generated, characterized, and selected to bind each and all of free cTn, binary complexed cTn and ternary complexed cTn, 4) the nature of the invention is a method capable of determining the presence or amount of all forms, i.e. free and complexed, of cTn using a cocktail of antibodies, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that shows generation, characterization, and selection of an antibody that has specific binding for each and all of free cTn, binary complexed cTn, and ternary complexed cTn , and lastly 7) the claims broadly recite a method for determining the presence or amount of all free and complexed forms of cTn using a single antibody that has specific binding for each and all of the free and complexed forms of cTn, without specifically stating how this can be done without undue experimentation.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

8. Applicant's arguments with respect to claims 85-96, 102-106, and 114-142 have been considered but are moot in view of the new ground of rejection.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
Patent Examiner
Art Unit 1641

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641